Respiratory Medicine Case Reports 18 (2016) 35–36

Contents lists available at ScienceDirect

Respiratory Medicine Case Reports

journal homepage: www.elsevier.com/locate/rmcr

Case report

Sulfasalazine: A rare cause of acute eosinophilic pneumonia

P. Nadarajan [a, *], A. Fabre [b], E. Kelly [a]

[a] Department of Respiratory Medicine, St. Vincent's University Hospital, Dublin, Ireland
[b] Department of Histopathology, St. Vincent's University Hospital, Dublin, Ireland

ARTICLE INFO

Article history:
Received 18 January 2016
Received in revised form
11 March 2016
Accepted 20 March 2016

Keywords:
Eosinophilic pneumonia
Interstitial lung disease
Drug induced lung disease

ABSTRACT

Sulfasalazine is a compound of 5-aminosalicylic acid (5-ASA) and sulfapyridine joined by an azo bond. It is a widely used drug in the treatment of chronic inflammatory bowel disease. Fatal toxicity of sulfasalazine arises from its effects on the bone marrow and the resulting blood dyscrasias. Pulmonary toxicity from sulfasalazine is a rather rare finding. Here, we present the case of a patient who developed acute eosinophilic pneumonia with sulfasalazine use.

1. Introduction

Sulfasalazine is a compound of 5-aminosalicylic acid (5-ASA) and sulfapyridine joined by an azo bond. It is a widely used drug in the treatment of chronic inflammatory bowel disease. Fatal toxicity of sulfasalazine arises from its effects on the bone marrow and the resulting blood dyscrasias [1]. Pulmonary toxicity from sulfasalazine is a rather rare finding. Acute eosinophilic pneumonia is characterized by the rapid accumulation of eosinophils in the lung in response to allergens, inflammation or infection. Symptom onset is usually rapid and can include dyspnoea, fever, cough and chest pain. Cigarette smoke, drugs and occupational factors have been shown to trigger acute eosinophilic pneumonia. Here, we report a patient who developed acute eosinophilic pneumonia with sulfasalazine use. This resolved completely with sulfasalazine withdrawal and treatment with oral corticosteroids.

2. Case report

A 44-year old woman with a background of ulcerative colitis presented to the Emergency Department with a 5-week history of fever, cough, dyspnoea and weight loss. She had been on Sulfasalazine for a 12-week period and Adalimumab, a tumour necrosis factor-alpha (TNF-α) antagonist. Both medications were held on admission. She was pyrexial (38.2 °C), tachypnoeic (respiratory rate of 20/min) with normal oxygen saturations on room air (98%). Physical examination revealed scattered crepitation over both lungs on auscultation. Blood tests showed a peripheral eosinophilia (0.6×10^9/L) and a raised C-reactive protein (CRP). An autoimmune screen was negative. Chest radiograph (Fig. 1) showed new, bilateral multilobar pulmonary infiltrates. Sputum culture was negative for pathogenic bacteria and acid-fast bacilli. A tuberculin-skin test was negative. She proceeded to have to fibreoptic bronchoscopy that was unremarkable. Bronchoalveolar lavage (BAL) (Fig. 2) was negative for infective aetiologies including viral, tuberculous and fungal infections. However, the differential cell count from the BAL showed 41% eosinophils. A diagnosis of Sulfasalazine-induced eosinophilic pneumonia was made based on our findings and a review of her medications. Oral corticosteroids were started and she improved significantly with gradual improvement in her respiratory symptoms. After consultation with the gastroenterologist, Adalimumab was restarted but the Sulfasalazine was discontinued. She was reviewed in the respiratory clinic 2 weeks later. Her chest radiograph (Fig. 3) had dramatically improved with near complete resolution of the bilateral pulmonary infiltrates.

3. Discussion

The sulfapyridine moiety in sulfasalazine, which acts as a carrier to transport 5-ASA to the colon, is believed to be responsible for

Abbreviations: ASA, Aminosalicylic Acid; BAL, Bronchoalveolar Lavage; CRP, C-reactive protein; MGG, May-Grunwald-Giemsa; TNF-α, Tumour necrosis factor alpha.

* Corresponding author. Department of Respiratory Medicine, Education & Research Centre, St. Vincent's University Hospital, Elm Park, Dublin 4, Ireland.
E-mail address: sonadarp2@yahoo.ie (P. Nadarajan).

http://dx.doi.org/10.1016/j.rmcr.2016.03.006

Fig. 1. Chest radiograph on admission.

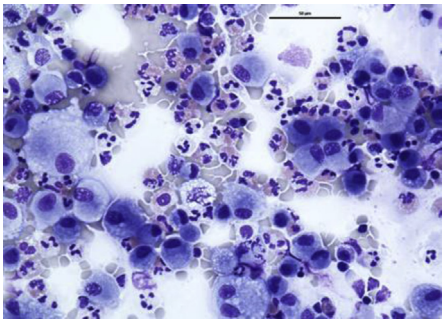

Fig. 2. Bronchoalveolar lavage cytology showing eosinophils (MGG stain).

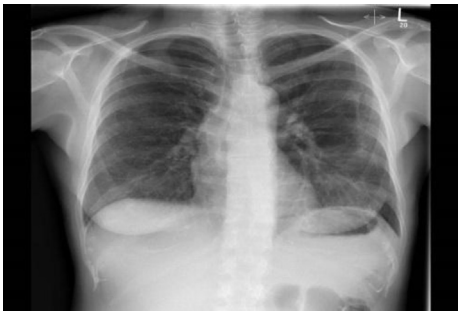

Fig. 3. Chest radiograph 2 weeks after treatment with oral corticosteroids.

most of the hypersensitivity reactions that occur. Pulmonary hypersensitivity reactions such as eosinophilic pneumonia, fibrosing alveolitis and bronchiolitis obliterans remain rare with use of sulfasalazine and are usually self-limiting. However there have been case reports with fatal outcomes, particularly in cases where the drug was not withdrawn [2,3]. We believe that sulfasalazine is the offending drug in our patient despite the time lag between commencing sulfasalazine and the onset of symptoms, as her symptoms appeared after sulfasalazine was administered, improved once sulfasalazine was discontinued and there are no other alternative causes that could have caused the reaction.

Eosinophilic pneumonia should be considered in patients who are on sulfasalazine treatment who present with pulmonary symptoms and abnormal chest radiography, accompanied by peripheral eosinophilia. The symptom triad of dyspnoea, cough and fever will occur in about 50% of cases [1]. BAL findings can support the diagnosis but the absence of eosinophils in the lavage fluid does not out rule eosinophilic pneumonia. The pulmonary symptoms mentioned above will resolve completely in a few weeks after withdrawal of the drug in the majority of cases. Although the evidence for corticosteroids in sulfasalazine induced lung toxicity is weak, a trial of systemic steroid therapy can be considered if the patient is very ill despite sulfasalazine withdrawal. There have been suggestions that a re-challenge or a provocation test is essential to establish a temporal relation, however given the significant morbidity of eosinophilic pneumonia and the availability of alternative 5-ASA agents such as mesalazine and olsalazine [4] for treatment of ulcerative colitis, we deemed this inadvisable in the case of this patient.

Conflict of interest

The authors have no conflicts of interest, direct or indirect, to declare.

Author contribution

1. Parthiban Nadarajan: Manuscript preparation, literature search, images.
2. Emer Kelly: Manuscript preparation, review of manuscript, literature search.
3. Aurelie Fabre: Data analysis, review of manuscript, images.

Funding

The authors wish to declare that we have not received any form of funding for our work.

References

[1] S.D. Parry, C. Barbatzas, E.T. Peel, J.R. Barton, Sulphasalazine and lung toxicity, Eur. Respir. J. 19 (2002) 756–764.
[2] D. Davies, A. MacFarlane, Fibrosing alveolitis and treatment with sulphasalazine, Gut 15 (1974) 185–188.
[3] J. Baillie, Sulfasalazine and pulmonary infiltrates, Am. J. Gastroenterol. 79 (1984) 77.
[4] J. Scherpenisse, P.D. van der Valk, J.M. van den Bosch, P.A. van Hees, J.H. Nadorp, J. Clin. Gastroenterol. 10 (2) (1988) 218–220.